

### Amendments to the Specification

Please replace the paragraph appearing at page 13, lines 1-3 with the following amended paragraph:

FIGURE 4C depicts the isolated DNA coding sequence for the *dnaX* gene (also present in FIGURES 4A and 4B ~~3A and 3B~~) in accordance with the invention, which corresponds to SEQ. ID. No. 3.

Please replace the paragraph appearing at page 75, lines 7-31 with the following amended paragraph:

The XbaI insert encoded an open reading frame, starting with a GTG codon, of 529 amino acids in length (58.0 kDa), closer to the predicted length of the *B. subtilis*  $\tau$  subunit (563 amino acids, 62.7 kDa mass)(Alonso et al., 1990) than the *E. coli*  $\tau$  subunit (71.1 kDa)(Yin et al., 1986). The *dnaX* gene encoding the  $\gamma/\tau$  subunits of *E. coli* DNA polymerase III holoenzyme is homologous to the *holB* gene encoding the  $\delta'$  subunit of the  $\gamma$  complex clamp loader, and this homology extends to all 5 subunits of the eukaryotic RFC clamp loader as well as the bacteriophage gene protein 44 of the gp44/62 clamp loading complex (O'Donnell et al., 1993). These gene products show greatest homology over the N-terminal 166 amino acid residues (of *E. coli dnaX*); the C-terminal regions are more divergent. ~~Fig. 4 shows~~ Figures 5A-B show an alignment of the amino acid sequence of the N-terminal regions of the *T.th. dnaX* gene product to those of several other bacteria. The consensus GXXGXGKT (SEQ. ID. No. 17) motif for nucleotide binding is conserved in all these protein products. Further, the *E. coli*  $\delta'$  crystal structure reveals one atom of zinc coordinated to four Cys residues (Guenther, 1996). These four Cys residues are conserved in the *E. coli dnaX* gene, and the  $\gamma$  and  $\tau$  subunits encoded by *E. coli dnaX* bind one atom of zinc. These Cys residues are also conserved in *T.th. dnaX* (shown in ~~Fig. 4~~ Figures 5A-B). Overall, the level of amino acid identity relative to *E. coli dnaX* in the N-terminal 165 residues of *T.th. dnaX* is 53 %. The *T.th. dnaX* gene is just as homologous to the *B. subtilis dnaX* (53 % identity) gene relative to *E. coli dnaX*. After this region of homology, the C-terminal region of *T.th. dnaX* shares 26% and 20% identity to *E. coli* and *B. subtilis dnaX*, respectively. A proline rich region, downstream of the conserved region, is also present in *T.th. dnaX* (residues 346-375), but not in the *B. subtilis dnaX* (see Figs. 3A and 3B). The overall identity between *E. coli dnaX* and *T.th. dnaX* over the entire gene is 34%. Identity of *T.th. dnaX* to *B. subtilis dnaX* over the entire gene is 28%.

Please replace the paragraph appearing at page 103, lines 15-25 with the following amended paragraph (note that underlining of the sequences appears in the original text):

The *Aquifex aeolicus holB* gene was not previously identified by the genome sequencing facility at Diversa (Deckert et al., 1998). The *Aquifex aeolicus holB* sequence was obtained by searching the *Aquifex aeolicus* genome with the sequence of the *T.th.*  $\delta'$  (encoded by *holB*). The *Aquifex aeolicus holB* gene was amplified by PCR using the following primers: the upstream 39mer (5'-GTGTGTCATATGGAAAAAGTTTTTTTGGAAA AA ACTCCAG-3') (SEQ. ID. No. 161) contains an NdeI site (underlined); the downstream 35mer (5'-GTGTGTGGATCCTTAATCCGCCTGAACGGCTAACG-3') (SEQ. ID. No. 162) contains a BamHI site (underlined). The PCR product was digested with NdeI and BamHI, purified, and ligated into the pET24 NdeI and BamHI site to produce pETAaholB.